

Please amend the specification as follows. In the abstract, replace the existing abstract with the following

Abstract

Polynucleotides directed towards a gene of a catalytic subunit of human telomerase and the use of polynucleotides directed towards a gene of a catalytic subunit of human telomerase for the diagnosis, prophylaxis, reduction and follow-up of diseases associated with cell growth, differentiation and/or division.

Please amend the specification by deleting present page 2 and inserting the following pages 2 and 2a in its place.

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scribed as a specific means for the therapeutic control of tumor cells. Important efforts in modifying the activity of telomerase in association with cancerous diseases have been disclosed in EP 666 313, WO 97/37691, WO 99/50279, US 2002/0045588 A1 or WO 98/28442. However, the above general teachings do not disclose any concrete teachings as to technical activity to a person skilled in the art. While a substance or a molecule interacting with the entire sequence region encoding hTERT will result in a reduction of the corresponding telomerase activity, e.g. in a cell culture, such substances, however, are not suitable for application in organisms because they are normally too large in size, being attacked and destroyed by the immune system of the respective organism. Moreover, a large number of undesirable interactions or side effects may occur. The object of the invention was therefore to provide alternative, compact molecules that would undergo facile and effectively inhibiting interaction with selected specific structural units encoding telomerase.

Summary of the Invention

The invention solves the above technical problem by providing a polynucleotide directed towards an mRNA of the catalytic subunit of human telomerase (hTERT), said polynucleotide undergoing specific interaction particularly with primary structures of said hTERT-mRNA in two target sequence regions, 2176 to 2250 and 2296 to 2393, according to the gene data base entry AF 015950. The numbers represent the corresponding nucleotide positions within the hTERT-mRNA (overall length: 4015 nucleotides), and this also applies to the following sections. Hence, the invention relates to the unexpected teaching that tumor-associated abnormal hTERT-mRNA expression patterns and telomerase activity levels can be counteracted by possible hTERT inhibition using the polynucleotides according to the invention. Said polynucleotides are directed towards well-defined hTERT-mRNA sequence motifs in a range of from 2000 to 2500. They may represent biological and/or chemical structures capable of interacting with the target sequence region in such a way that specific recognition/binding and interaction can be determined. More specifically, examples of polynucleotides can be nucleic acid

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constructs and derivatives thereof. Of course, it is also possible to use other recognition molecules such as antibodies, lectins, Affilines, aptamers, chelators and others instead of or in combination with said polynucleotides.

Brief Description of the Drawings

Figure 1 is a cartoon showing an AS-ODN against local secondary structures of the hTERT-mRNA.

Figure 2 is a graphical representation of the influence of multiple anti-hTERT treatments with various AS-ODNs on the viability of EJ28 cells.

Figure 3 is a graphical representation of the effects of two AS-ODN transfections on the colony-forming behavior of EJ28 cells.

Figure 4 is a graphical representation of the relative expression level of AS-ODN-treated EJ28 cells.

Figure 5 is a graphical representation of the effect of combination treatment of the BCa cell line with various reagents.

Detailed Description of the Invention

In a particularly preferred embodiment the polynucleotide specifically interacts with two target sequence regions, 2176 to 2250 and 2296 to 2393. Advantageously, particularly efficient inhibition of hTERT is possible in these sequence regions. Likewise preferred are shorter regions having changes within said target sequences or changed peripheral